

## Arsenic and Diabetes: Assessing Risk at Low-to-Moderate Exposures

Nate Seltenrich

<https://doi.org/10.1289/EHP3257>

Long-term exposure to inorganic arsenic through drinking water and food is known to cause skin lesions and carry an elevated risk of cancer, among other health effects.<sup>1,2</sup> There is also evidence that high levels of exposure might increase an individual's risk of type 2 diabetes.<sup>3</sup> The connection is less clear at the low-to-moderate arsenic levels common in groundwater across the United States,<sup>4</sup> but a prospective study in *Environmental Health Perspectives* takes a step toward clarifying the relationship.<sup>5</sup>

Once ingested, inorganic arsenic is metabolized into various organic compounds, including monomethylarsenate (MMA) and dimethylarsinate (DMA). The proportions of inorganic arsenic, MMA, and DMA in an individual's urine can tell researchers something of the individual's risk for certain diseases. The presence of a high percentage of MMA (indicating lower methylation capacity) is a risk factor for cardiovascular disease, skin and bladder cancers, and the skin lesions that characterize highly exposed individuals, whereas a high percentage of DMA (indicating greater methylation capacity) has been associated with increased risk of diabetes.<sup>6</sup>

Researchers led by senior author Ana Navas-Acien, a professor of environmental health sciences at Columbia University,

assessed the relationship between arsenic exposure and incidence of type 2 diabetes among 1,838 American Indian men and women. The participants, members of the Strong Heart Family Study, lived in 12 communities in Arizona, Oklahoma, and North and South Dakota. American Indians are highly susceptible to type 2 diabetes due to a mix of genetic, lifestyle, and, potentially, environmental factors.<sup>7</sup>

The participants in this study had a median age of 36 years, allowing the researchers to assess the relationship between arsenic and type 2 diabetes early in the typical course of the disease. None of the individuals had diabetes at the start of the study. Baseline data were collected in 1998–1999 and 2001–2004, with follow-up occurring in 2001–2004 and 2006–2009.

To assess exposure, the researchers measured concentrations of different arsenic species in the participants' urine. This approach has the benefit of capturing arsenic intake via both water and foods, including rice, other grains, and fruit juices,<sup>8</sup> but it does not allow for direct comparison with regulatory guidelines for drinking water. Both the United States and the World Health Organization have adopted a drinking water standard of 10 µg/L (10 ppb),<sup>1,9</sup> but food levels currently are not regulated. The U.S. Food and Drug



Although maximum contaminant levels have been set for arsenic in drinking water, food levels are not regulated. However, U.S. and European food agencies are considering ways to limit people's dietary intake of arsenic, which may play a relatively large role in some populations' overall exposures. Image: © Coast-to-Coast/iStockphoto.

Administration has proposed nonbinding action levels of 10 ppb arsenic for both infant rice cereal<sup>10</sup> and apple juice.<sup>11</sup> The European Union also does not have binding limits for arsenic in food,<sup>12</sup> although in 2015 the European Commission called for member states to monitor arsenic in a variety of foods, including those intended for infants and young children.<sup>13</sup>

The median urinary arsenic level within the study population was 4.4 µg total arsenic (i.e., all species combined) per gram creatinine, representing low-to-moderate exposures. Still, among the 1,376 participants with no evidence of diabetes or prediabetes at the start of the study, individuals in the top tertile of exposure (urinary arsenic above 7.2 µg/g) were estimated to be twice as likely to develop diabetes during the study period as individuals in the lowest tertile of exposure (urinary arsenic below 2.9 µg/g).

The investigators found a higher percentage of DMA in the participants' urine, reflecting the association between higher methylation capacity and increased risk of diabetes. "Additional research is needed to understand the reasons for this finding with diabetes, as it is an opposite pattern compared to other arsenic-related outcomes such as cancer," says Navas-Acien.

Michelle Mendez, a professor of environmental and occupational health at the University of Pittsburgh, published a study of arsenic and diabetes in Mexico that found a similar relationship between moderate levels of exposure and markers of cardiometabolic risk.<sup>14</sup> She says the new findings suggest that regulation of arsenic in drinking water alone may not be sufficient to protect public health.

"These are pretty low levels of exposure that may, at the population level, have some adverse impacts," she says. "A lot of [arsenic exposure] may come from food at that level of exposure, and all the [tap water] filtration in the world will not help you if it is coming from food rather than water." Mendez was not involved in the current study.

There is evidence that B vitamins can help the body break down arsenic into a more rapidly excretable form, potentially reducing harmful effects.<sup>15,16</sup> Sung Kyun Park, a University of Michigan professor of epidemiology and environmental health science who also was not affiliated with the study, says that due to the relative ubiquity of arsenic in groundwater and some foods, more research into arsenic metabolism and nutritional supplementation is needed.

"The study of toxicant–nutrient interaction has important public health implications," Park says. The findings of such research, if validated, could potentially be translated into an economical intervention or population-wide recommendation to mitigate adverse health effects among exposed populations.

**Nate Seltenrich** covers science and the environment from Petaluma, California. His work has appeared in *High Country News*, *Sierra*, *Yale Environment 360*, *Earth Island Journal*, and other regional and national publications.

## References

1. WHO (World Health Organization). 2017. Arsenic. <http://www.who.int/media/centre/factsheets/fs372/en/> [accessed 11 December 2017].
2. Naujokas MF, Anderson B, Ahsan H, Aposhian HV, Graziano JH, Thompson C, et al. 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. *Environ Health Perspect* 121(3):295–302, PMID: 23458756, <https://doi.org/10.1289/ehp.1205875>.
3. Maull EA, Ahsan H, Edwards J, Longnecker MP, Navas-Acien A, Pi J, et al. 2012. Evaluation of the association between arsenic and diabetes: a National Toxicology Program workshop review. *Environ Health Perspect* 120(12):1658–1670, PMID: 22889723, <https://doi.org/10.1289/ehp.1104579>.
4. Ryker SJ. 2001. Mapping arsenic in groundwater—a real need, but a hard problem. *Geotimes* 46 (11):34–36.
5. Grau-Perez M, Kuo CC, Gribble MO, Balakrishnan P, Jones Spratlen M, Vaidya D, et al. 2017. Association of low-moderate arsenic exposure and arsenic metabolism with incident diabetes and insulin resistance in the Strong Heart Family Study. *Environ Health Perspect* 125(12):127004, <https://doi.org/10.1289/EHP2566>.
6. Kuo CC, Moon KA, Wang SL, Silbergeld, E, Navas-Acien A. 2017. The association of arsenic metabolism with cancer, cardiovascular disease, and diabetes: a systematic review of the epidemiological evidence. *Environ Health Perspect* 125(8):087001, PMID: 28796632, <https://doi.org/10.1289/EHP577>.
7. Welty TK, Coulehan JL. 1993. Cardiovascular disease among American Indians and Alaska Natives. *Diabetes Care* 16(11):277–283, PMID: 8422792.
8. Consumer Reports. 2014. FDA Data Show Arsenic in Rice, Juice, and Beer. <https://www.consumerreports.org/cro/news/2014/01/fda-data-show-arsenic-in-rice-juice-and-beer/index.htm> [accessed 11 December 2017].
9. U.S. EPA (Environmental Protection Agency). 2017. Chemical Contaminant Rules. <https://www.epa.gov/dwreginfo/chemical-contaminant-rules> [accessed 11 December 2017].
10. U.S. FDA (Food and Drug Administration). 2016. Inorganic Arsenic in Rice Cereals for Infants: Action Level Guidance for Industry. Draft Guidance. <https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM493152.pdf> [accessed 11 December 2017].
11. U.S. FDA. 2013. Draft Guidance for Industry: Arsenic in Apple Juice—Action Level. <https://www.fda.gov/RegulatoryInformation/Guidances/ucm360020.htm> [accessed 11 December 2017].
12. EFSA (European Food Safety Authority). 2009. Scientific Opinion on Arsenic in Food. *EFSA J* 7(10):1351, <https://doi.org/10.2903/j.efsa.2009.1351>.
13. European Commission. 2015. Commission Recommendation (EU) 2015/1381 of 10 August 2015 on the Monitoring of Arsenic in Food. *Off J Eur Union*. L213/9. <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015H1381&from=EN> [accessed 11 December 2017].
14. Mendez MA, González-Horta C, Sánchez-Ramírez B, Ballinas-Casarrubias L, Cerón RH, Morales DV, et al. 2016. Chronic exposure to arsenic and markers of cardiometabolic risk: a cross-sectional study in Chihuahua, Mexico. *Environ Health Perspect* 124(1):104–111, PMID: 26068977, <https://doi.org/10.1289/ehp.1408742>.
15. Gamble MV, Liu X, Ahsan H, Pilsner JR, Ilievski V, Slavkovich V, et al. 2006. Folate and arsenic metabolism: a double-blind, placebo-controlled folic acid-supplementation trial in Bangladesh. *Am J Clin Nutr* 84(5):1093–1101, PMID: 17093162.
16. Kordas K, Queirolo EI, Mañay N, Peregalli F, Hsiao PY, Lu Y, et al. 2016. Low-level arsenic exposure: nutritional and dietary predictors in first-grade Uruguayan children. *Environ Res* 147:16–23, PMID: 26828624, <https://doi.org/10.1016/j.envres.2016.01.022>.